REMARKS

Claims 1, 2, 6, 8-16, 28, 29, and 31-36 are pending in the above-identified patent application. Claims 1, 6, 8-10, 12-14, 31, 33, 35 and 36 are amended herein. Claims 2, 3-5, 7, 17-27 and 30 are canceled. No new matter is introduced, and Applicants' amended claims are fully supported by Applicants' specification.

1. Restriction/Election

Applicants confirm the election without traverse of Group I where R^5 = piperazines (Z = N and r = 2). The claims have been amended herein to conform to Applicants' elected subject matter.

Applicants note the possibility of rejoinder of method claims 33-36 that are commensurate in scope with claim 1 in the event that claim 1 is deemed allowable. While claims 33-36 are considered withdrawn from examination at present, Applicants have amended independent claims 33, 35 and 36 to make them dependent upon claim 1 to facilitate possible rejoinder.

2. Abstract

The Examiner objected to the Abstract because it did not describe the intended use of the compounds. Applicants have accordingly provided a new Abstract which states the intended use of the claimed compounds.

3. Rejection of Claims Under 35 USC §112, First Paragraph

The Examiner rejected claims 1-30 and 32 under 35 USC §112, first paragraph for failing to comply with the enablement requirement. The Examiner stated, inter alia, that:

the scope of piperazines claimed is not adequately enabled;

that the nature of rings permitted at R2 are mono- and polyfused carbocyclics as well as hetero-containing rings which can in turn be substituted with a variety of groups including "acyl" of non-limiting scope; and

that R1 includes "heteroalkyl" where up to three hetero-containing moieties can be present which in turn may be alkylated or acylated.

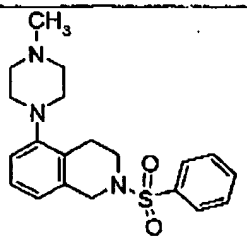
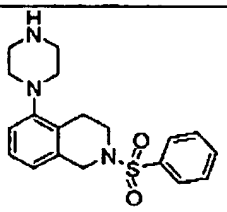
Applicants address each of these items below.

PAGE 13/17 * RCVD AT 5/16/2006 5:40:35 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-3/8 * DNIS:2738300 * CSID:650 855 5322 * DURATION (mm-ss):04-24

a. Scope of the claimed piperazines

Claim 1 as amended recites piperazine, attached at the N-position (1-position), with R^6 through R^{10} each independently being hydrogen or alkyl. The breadth of Applicants' claims regarding piperazines is thus limited in scope to piperazin-1-yl, substituted with hydrogen or alkyl.

Applicants first note that skilled persons recognize that interchanging of hydrogen and lower alkyl (i.e., homologs) on a compound will generally result in compounds with similar properties. *In re Payne*, 606 F.2d 303, 313, 203 USPQ 245, 254 (CCPA 1979), MPEP §2144.09 Compounds 1 and 2 (shown below) of Table 1 of Applicants' specification are hydrogen-methyl analogs for the variable R^{10} are provided as a working example of hydrogen/alkyl-substituted piperazinyl analogs. Unsurprisingly, these two compounds have very similar 5-HT6 activity (pKi = 8.58 and 8.38 respectively).

	Name (Autonom®)	Structure	Example	M+H	pKi 5-HT6
1	2-Benzenesulfonyl-5-(4-methylpiperazin-1-yl)-1,2,3,4-tetrahydroisoquinoline		1	371	8.38
2	2-Benzenesulfonyl-5-piperazin-1-yl-1,2,3,4-tetrahydroisoquinoline		1	356	8.58

While Applicants have not made alkyl analogs for variables R^6-R^9, Applicants believe that, like R^{10}, such hydrogen-alkyl analogs will have similar properties. The Applicants thus respectfully submit that the level of unpredictability is low to the piperazinyls recited by Applicants, and that the corresponding alkyl analogs for R^6-R^9 will have properties similar to the hydrogen analogs.

Applicants further note that the "Buchwald" reaction of Example 1, step 2 is well known and has been used to make a variaty of aryl amines (see, e.g., US 5576460) from various aryl substrates and at various positions on such substrates. US 5929281 more particularly notes that the Buchwald reaction may be used with 2-methyl-piperazine, 2-6-

PAGE 14/17 * RCVD AT 5/16/2006 5:40:35 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-3/8 * DNIS:2738300 * CSID:650 855 5322 * DURATION (mm-ss):04-24

dimethylpiperazinc as well as substituted morpholines, pyrrolidines and piperidines (col. 4 lines 45-55). Further, 2, 6-dimethyl-piperazine (Aldrich **D18,030-0**) and 2-methylpiperazine (Aldrich **39-716-4**) are commercially available. Thus, using well known chemistry and commercially available reactants, skilled persons could make additional alkyl-substituted piperazinyl compounds in accordance with Applicants' claimed invention.

Because of the demonstrated predictability of results with hydrogen/alkyl piperazinyl analogs, the chemistry known in the art and the commercially available substituted piperazines, Applicants believe that the scope of the claimed piperazines in Applicants claims is fully enabled.

b. Nature of rings permitted at R^2

The Examiner indicated that the nature of rings permitted at R^2 includes mono- and polyfused carbocyclics as well as hetero-containing rings which can in turn be substituted with a variety of groups including "acyl" of non-limiting scope. Applicants have amended claim 1 to limit R^2 to "aryl" only. Applicants specification exemplifies both phenyl and naphthyl compounds as shown in Table 1.

c. R^1 includes "heteroalkyl"

The Examiner indicated that the recitation of "heteroalkyl" with regard to variable R^1, where up to three hetero-containing moieties can be present which in turn may be alkylated or acylated, was not enabled by Applicants' specification. Applicants have amended claim 1 delete the recitation of "heteroalkyl" from the variable R^1. Applicants have also deleted recitation of non-excemplified groups $-SO_2-NR^eR^f$, $-N(R^e)-C(=O)-R^f$, and $-C(=O)\ R^e$ from R^1.

Accordingly, Applicants believe that amended claim 1 and its dependend claims meet the criteria of 35 USC §112 first paragraph.

4. Rejection of Claims Under 35 USC §103

Claims 1-3, 5, 17-19, 21, 23-28, 30-32 were rejected under 35 USC §103 as being unpatentable over Okhura WO'135 (US '362). The Examiner stated that Ohkura et al. describes compounds where Y is CR^aR^b and X is C(O), for uses based on lipid-lowering activity. The Examiner noted compounds in columns 89-96 in particular noting that

PAGE 15/17 * RCVD AT 5/16/2006 5:40:35 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-3/8 * DNIS:2738300 * CSID:650 855 5322 * DURATION (mm-ss):04-24

Ohkura's exemplified compounds differ by 1) being attached at the 7- compound vis the 5- or 6- position (as in Applicants' compounds) and 2) are substituted at the 4-piperazine position with diphenylmethyl (3,3-diphenyl-propan-1-yl) rather than alkyl. The Examiner stated that Ohkura teaches that the piperazinyl group may be at any location of the benzene portion of the ring system, that the definition of "X-Y-Z-" encompasses "alkyl", and that it would be obvious to skilled persons at the time of invention to expect corresponding isomers of the Okhura compounds having alkylation of the piperazine ring to also be useful as lipid-lowering agents.

Applicants have amended claim 1 to delete recitation of X = CR^aR^b and Y = C(O). Claim 31 has been amended to delete the 19th and 20th compounds, and claims 5, 17-27 and 30 have been canceled The Examiner noted that the elected species corresponding to Y = $-SO_2-$ is not taught or suggested by the art of record. Accordingly, claim 1 as amended and the claims depending therefrom are believed by Applicants to be patentable over Ohkura.

5. Objections Under 37 CFR §1.75(c)

The Examiner objected to claims 14-16 and 25-27 as being in improper form because a multiple dependent claim cannot refer back to different sets of claims to different features.

No claims in the above-identified patent application are in multiple dependent format.

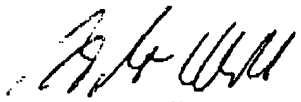
PAGE 16/17 * RCVD AT 5/16/2006 5:40:35 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-3/8 * DNIS:2738300 * CSID:650 855 5322 * DURATION (mm-ss):04-24

CONCLUSION

In view of the foregoing amendments and remarks, the Applicants respectfully believe that all claims pending in the above-identified case are now in condition for allowance. If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-354-7540.

No fees should be due. However, in the event it is determined that a fee is due, please charge same to Deposit Account No. 18-1700.

Respectfully submitted,



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PAGE 17/17 * RCVD AT 5/16/2006 5:40:35 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-3/8 * DNIS:2738300 * CSID:650 855 5322 * DURATION (mm-ss):04-24